Title: Antioxidant And Radical... Inventor: Raymond J. Bergeron, Jr.

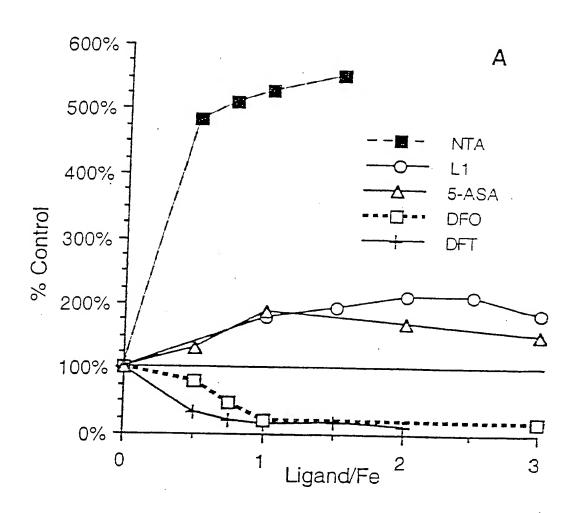


FIG. 1A

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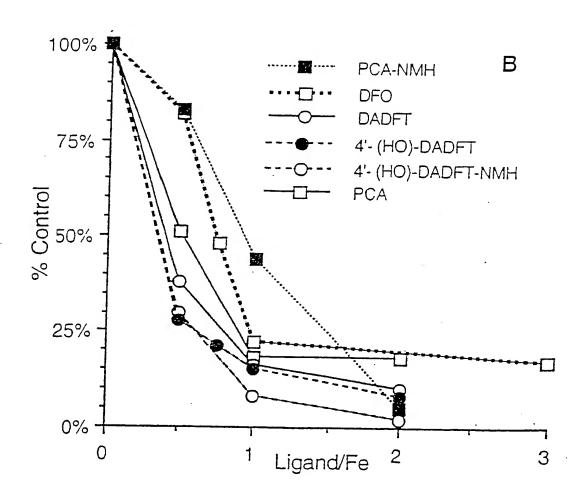


FIG. 1B

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## Control



FIG. 2

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FIG. 3

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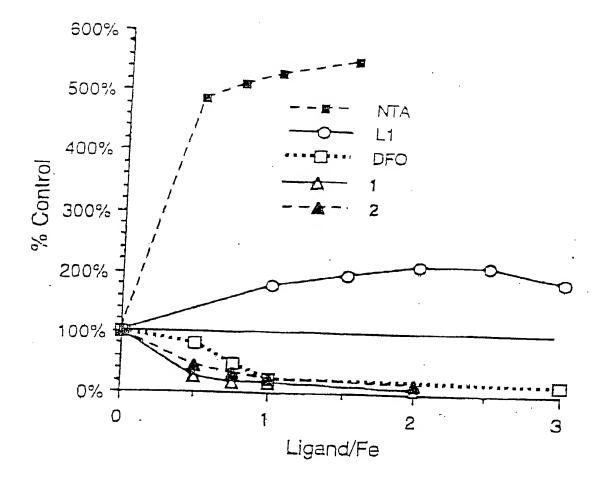


FIG. 4

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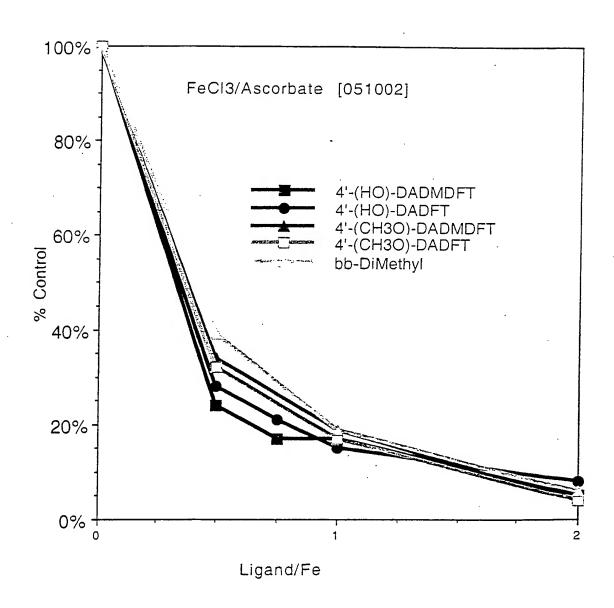


FIG. 5

Inte.

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Compound	Slope x 10 <sup>3</sup> OD units/µM*
DFT	-0.9
DMIDFT	-1.3
PCA	-3.3
DADFT	-25.1
DADMDFT	-28.1
5-ASA	-34.4
PCA-NMH	-34.6
Trolox	-36.6
DMDFT-NMH	-47.4
L1	-52.9
4'-(HO)-DADMDFT	-101.6
4'-(HO)-DADFT	-105.6
4'-(HO)-DADMDFT-NMH	-135.5
DFO	-136.8
4'-(HO)-DADFT-NMH	-141.4

<sup>\*</sup>The slope was derived from  $A_{734}$  vs time data over a six-minute reaction period between the chelator of interest and the 2,2'-azinobis(3-ethylbenzothiazoline-6-sulfonic acid) radical cation (ABTS $^{+}$ ), which was formed from the reaction between ABTS and persulfate. A negative slope represents a decrease in the amount of highly colored radical cation over the time interval. Trolox, an analog of Vitamin E, served as a positive control.

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Damage P vs Pvs **MPO** P vs Pvs Compound\* Ν (%) Ť control: parent§ controlf parents activity Control (no acid) 10 4 ± 5 < 0.001 N/A\*\* **4494** ± **2254** < 0.001 N/A Control 4% acetic acid 13 65 = 18N/A N/A 91479 = 84927 NiA N/A DMDFT-NMH 10 22 = 17< 0.001 <0.001 14406 ± 8683 < 0.005 10.0> DMDFT 10  $61 \pm 15$ N.S. †† N/A  $39229 \pm 27109$ < 0.05 N/A 45 ± 24 (DMDFT-NMH),/Fe 9 <0.05 <0.02 \* \* 54370 ± 18749 N.S. <0.00111 PCA 10  $44 \pm 11$ < 0.001 N/A 29942 ± 11255 < 0.02 N/A PCA-NMH 9 38 = 18< 0.002 N.S. 23642 ± 14341 <0.01 N.S. 4'-(HO)-DADMDFT 10 57 = 15N.S. N/A 56466 ± 52617 N.S. N/A 4'-(HQ)-DADMDFT-NMH 39 ± 11 10 < 0.001 < 0.005  $18426 \pm 20930$ < 0.005 <0.05 DFO 9  $39 \pm 15$ < 0.001 N/A 20049 = 17314< 0.01 N/A 4'-(HO)-DADFT 62 = 10N.S. N/A 64192 = 30802N.S. N/A 4'-(HO)-DADFT-NMH 46 = 23<0.05 8 =0.05 41021 = 35525<0.05 N.S. Rowasa@§§ 62 = 19N.S. N/A 51805 = 38165N/A

<sup>\*</sup>All chelators (2 ml) were administered intracolonically at a dose of 650 µmol kg<sup>-1</sup>. Rowasa® (2 ml, 66.7 mg ml<sup>-1</sup> 5-ASA) was given intracolonically at a dose of 2318 µmol kg<sup>-1</sup>.

<sup>†</sup>Percent damage in scanned images of the colons was measured with the aid of the Adobe Photoshop program; the mean percentage of the image scored as "damaged" (as detailed in the Experimental Section) ± standard deviation is reported.

<sup>‡</sup>P versus 4% acetic acid control animals.

 $<sup>\</sup>delta P$  versus animals treated with the respective carboxylic acid.

<sup>¶</sup> Myeloperoxidase (MPO) activity expressed as mAU min<sup>-1</sup> g of colonic tissue<sup>-1</sup>, mean ± standard deviation.

<sup>\*\*</sup>N/A, not applicable.

<sup>††</sup>N.S., not significant (P > 0.05)

<sup>‡‡</sup>In this instance, P versus animals treated with free, uncomplexed DMDFT-N.

<sup>§§</sup>The pharmaceutical preparation, which contains 5-ASA (66.7 mg ml<sup>-1</sup>), was tested in the rodents.

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Compound	slope x 10 <sup>3</sup> OD units/μM <sup>a</sup>
Trolox	-37°
Li	-53 <sup>b</sup>
4'-(OH)-DADMDFT	-1026
BDU	-136
DFO	-137 <sup>b</sup>
-	

<sup>&</sup>quot;The slope was derived from  $A_{734}$  vs time data over a 6-min reaction period between the chelator of interest and the 2,2'-azinobis(3-ethylbenzothiazoline-6-sulfonic acid) radical cation (ABTS $^{-}$ ), which was formed from the reaction between ABTS and persulfate. A negative slope represents a decrease in the amount of highly colored radical cation over the time interval. Trolox, an analogue of vitamin E, served as a positive control.

<sup>&</sup>lt;sup>b</sup> Bergeron, R.J.; Wiegand, J.; Weimar, W.R.; Nguyen, J.N.; Sninsky, C.A., unpublished results.

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compound	slope × 10 <sup>3</sup> OD units/µM"
4'-(CH;O)-DADMDFT	-33
4'-(CH <sub>3</sub> O)-DADFT	-36
Trolox	<b>-</b> 37 <sup>-</sup>
β,β-Dimethyl	<b>-</b> 70
4'-(HO)-DADMDFT	-102
4'-(HO)-DADFT	-106

<sup>&</sup>lt;sup>a</sup> The slope was derived from  $A_{734}$  vs time data over a 6-min reaction period between the chelator of interest and the 2.2'-azinobis(3-ethylbenzothiazoline-6-sulfonic acid) radical cation (ABTS'\*), which was formed from the reaction between ABTS and persulfate. A negative slope represents a decrease in the amount of highly colored radical cation over the time interval from an initial  $OD_{470}$  of 1.000. Trolox, an analogue of vitamin E, served as a positive control.